PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing 21 April 2005 (21-04-2005)
(day/month/year)

Applicant's or agent's file reference
TV/11830.102

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA2004/002118	13 December 2004 (13-12-2004)	12 December 2003 (12-12-2003)

International Patent Classification (IPC) or both national classification and IPC
IPC[7]: C12Q-1/68

Applicant
INFECTIO RECHERCHE INC. ET AL

1. This opinion contains indications relating to the following items :

[X]	Box No. I	Basis of the opinion
[X]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[X]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement.
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA	Authorized officer
Canadian Intellectual Property Office *Place du Portage I, C114 - 1st Floor, Box PCT* *50 Victoria Street* *Gatineau, Quebec K1A 0C9* Facsimile No: 001(819)953-2476	Qianfa Chen (819) 994-1374

Box No. I **Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] This opinion has been established on the basis of a translation from the original language into the following language ,which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

   a. type of material

      [ ] a sequence listing

      [ ] table(s) related to the sequence listing

   b. format of material

      [ ] in written format

      [ ] in computer readable form

   c. time of filing/furnishing

      [ ] contained in the international application as filed.

      [ ] filed together with the international application in computer readable form.

      [ ] furnished subsequently to this Authority for the purposes of search.

3. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statement that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

An invitation (Form PCT/ISA/ 225) was sent to the applicant to furnish to this Authority a nucleotide Sequence Listing on March 18, 2005. Applicant has requested an extension of time in order to file the Sequence Listing on April 14, 2005. This international search report has been established without regard to any nucleotide sequences disclosed in the international application.

Box No. II Priority

1. [ ] The following document has not yet been furnished :

   [ ] copy of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(a)).

   [ ] translation of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. [ ] This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary :

   It has not yet been possible to consider the validity of the priority claim because the Authority does not have in its possession a copy of the earlier application whose priority has been claimed. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

Box No. IV Lack of unity of invention

1. [ ] In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has :

   [ ] paid additional fees

   [ ] paid additional fees under protest

   [ ] not paid additional fees

2. [ ] This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   [X] complied with

   [ ] not complied with for the following reasons :

4. Consequently, this opinion has been established in respect of the following parts of the international application :

   [X] all parts

   [ ] the parts relating to claim Nos. _____

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	3-12, 14-16, 20-22, 25, 29-38, 40-42, 45-47, 51 and 55-57	YES
	Claims	1, 2, 13, 17-19, 23, 24 (1st and 2nd), 26-28, 39, 43, 44, 48-50 and 52-54	NO
Inventive step (IS)	Claims		YES
	Claims	1-57	NO
Industrial applicability (IA)	Claims	1-57	YES
	Claims		NO

2. Citations and explanations :

Reference is made to the following documents:

D1. US 2003/0152995 A1 (HANNAH, E.), 14 August 2003

D2. US 2002/0068295 A1 (MADOU, M. et al.), 6 June 2002

D3. US 6,589,731 B1 (CHEN, L. et al.), 8 July 2003

D4. US 6,197,949 B1 (TEOULE, R. et al.), 6 March 2001

D5. WO 02/095052 (HYLDIG-NIELSEN, J. et al.), 28 November 2002

D6. NILSSON, K. et al. (A). Proc. Natl. Acad. Sci. U.S.A., 2 September 2003, Vol.100, No.18, Pages 10170-10174

D7. NILSSON, K. et al. (B). Nature Materials, June 2003, Vol.2, Pages 419-424

D8. WO 02/081735 A3 (LECLERC, M. et al.), 17 October 2002

D9. NIELSEN, P. et al. Current Issues Molec. Biol., 1999, Vol.1, No.2, Pages 89-104

D10. US 2002/0177136 A1 (MCBRANCH, D. et al.), 28 November 2002

D11. DORÉ, K. et al. J. AM. Chem. Soc. 7 April 2004, Vol.126, No.13, Pages 4240-4244

D1 describes an apparatus, composition and related method for sequencing a target nucleic acid using peptide nucleic acids (PNAs) as neutral probes (paragraph 55), wherein one or more labels may be attached to each probe. A label may be detected by using a variety of means, such as spectrophotometer, luminometer, NMR, mass-spectroscopy, imaging systems, photo multiplier tube, and/or other appropriate standard detection means. In certain embodiments conductive polymers may be used as label. Conductive polymers are tunable to unique spectroscopic profiles based on the polymer composition, length, side chain groups and/or dopants. (paragraph 58). Typical conductive polymers include, but not limited to polyaniline, polyphenylene-vinylene, polythiophene (paragraph 63).

D2 describes a micro-machined and nanomachined device or system using multimeric biopolymers to sense the presence of a target analyte, to actuate a response to the presence of the target analyte, e.g. nucleotides. The multimeric biopolymers comprise at least two monomeric units. The monomeric units are selected from the group consisting of full-length proteins, polypeptides, nucleic acid molecules and peptide nucleic acids (paragraphs 5, 22 and 23). Redox polymers, such as polypyrrole, polyaniline and polythiophene, are used to sense the conformational change of the multimeric biopolymer upon binding to the target analyte (paragraphs 54 and 55).

(Continuation on Supplemental Box)

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

D. Description Defects:

A statement in an application, such as found on page 6, line 9, and page 21, line 6, which incorporates by reference any other document, does not comply with Article 5 PCT (4.26 PCT International Search and Preliminary Examination Guidelines).

The description does not comply with PCT Rule 5.1(a)(ii). Specifically, all documents referred to in the description must be available to the public. Reference to the documents on page 5, lines 11 and 21, page 9, line 31, and page 27, line 16, must be deleted or replaced by their corresponding publication numbers.

E. Claim Defects:

Claims 1, 27 and 53 are broader in scope than the teaching of the description and do not comply with Article 6 PCT. The expression "uncomplexed neutral capture probes" encompasses probes that are not contemplated in the description by the applicant. The description only describes the use of peptide nucleic acids or methylphosphonates as the neutral capture probe. Therefore, applicant should defined the "neutral capture probes" accordingly.

Claims 1, 27 and 53 do not comply with Article 6 PCT. A metal atom, a molecule and a macromolecule cannot be appropriate members of a single group.

Claim 24 does not comply with Article 6 PCT. There are two claims numbered as claim 24.

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation Box V (page 1 of 3)

D3 describes a method for detecting a biological agent by contacting a sample with a sensor including a polymer capable of having an alterable measurable property from the group of luminescence and electrical conductivity. The polymer consists of a recognition element, a tethering element and a property-altering element bound thereto as to alter the measurable property (column 2, lines 12-25). The recognition element of the sensor includes peptide nucleic acids (claim 10). The polymer used can be a luminescent molecule such as a fluorescent molecule or can be a conductive molecule. Suitable luminescent polymers can include luminescent conjugated material such as polythiophene (column 4, line 13-18). The detected biological agent can be taken from the group consisting of proteins, amino acids and oligonucleotides (column 4, lines 49-51).

D4 describes a method for detecting hybridization of nucleic acids using a copolymer (column 2, lines 5-19) comprising an electrically conductive polymer, e.g., polythiophene (column 2, lines 56-61), and a nucleotide, an oligonucleotide or one of the analogues thereof, e.g., analogues of the sugar-phosphate chain such as mono- or dithiophosphates, methylphosphonates and phosphotriesters (column 6, lines 28-35).

D5 describes the detection of target nucleic acids using peptide nucleic acid (PNA) as probe (abstract and page 2, lines 20-25), wherein the detectable moieties that can be used to label PNA probes can include an enzyme, such as alkaline phosphatase (page 8, line 14 to page 9, line 2).

D6 describes the conformational transitions of a water-soluble, zwitterionic, electroactive, and photoactive polythiophene derivative induced by noncovalent coupling of synthetic peptides designed to adopt alternative conformation (page 10170, right column, lines 28-32). The conformational changes in synthetic peptides including negatively charged peptides, positively charged peptides and neutrally charged peptides (i.e., an equal mole of negatively charged peptides mixed with an equal mole of positively charged peptides) can be detected by the optical measurement of the emission spectra of a photoactive polythiophene derivative added to the peptides (Fig. 2). The method described can be used for a wide range of different biosensors and for the design of novel bioelectronic devices (page 10174, right column, lines 2-5). D6 does not describe the use of peptide nucleic acids as capture probes.

D7 describes a method for the fluorometric detection of DNA hybridization on a chip or in solution based on the non-covalent coupling of DNA probes (single stranded or double-stranded) to a water-soluble zwitterionic polythiophene derivative (abstract). D7 does not describe the use of peptide nucleic acids as capture probes.

D8 describes a method allowing for the simple optical and electrochemical detection of double stranded oligonucleotides based on different electrostatic interactions between a water-soluble, cationic polythiophene derivative and single-stranded or double-stranded (hybridized) oligonucleotides (abstract). D8 does not describe the use of peptide nucleic acids as capture probes.

D9 describes a wide range of applications of PNAs. The unique chemical, physical and biological properties of PNAs (e.g., neutral backbone, stronger binding between complementary PNA/DNA strands than complementary DNA/DNA strands, and significantly increased rate of hybridization, p91, lines 18-22 and p93, lines 4 and 5) have been exploited to produce powerful biomolecular tools, antisense and antigene agents, molecular probes and biosensors (abstract).

D10 describes the use of PNAs as fluorescent biosensors for the specific detection of DNA and RNA (paragraphs 3, 25 and 27-30).

(Continuation on Supplemental Box)

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Box V (page 2 of 3)

D11 describes the specific detection of a few hundred molecules of genetic material using a fluorescent polythiophene biosensor.

A. Novelty

Claims 1, 2, 13, 17-19, 23, 24 (1st), 26-28, 39, 43, 44, 48, 49 and 52-54 lack novelty and do not comply with Article 33(2) of the *Patent Cooperation Treaty (PCT),* as being anticipated by D1, D2, D3, or D4. The cited documents independently describe the detection of target nucleic acids using peptide nucleic acids (PNAs) (D1, D2 and D3) or oligonucleotide analogues (e.g., methylphosphonates, D4) as the capture probes wherein the presence of the targets is visualised with a conductive polymer polythiophene or derivative thereof as reporter. Therefore, claims 1, 2, 13, 17-19, 23, 24 (1st), 26-28, 39, 43, 44, 48, 49 and 52-54 are not novel in view of D1, D2, D3, or D4.

Claims 24 (2nd) and 50 lack novelty and do not comply with Article 33(2) of the *Patent Cooperation Treaty (PCT),* as being anticipated by D5. D5 describes the detection of target nucleic acids using a peptide nucleic acid (PNA) as probe, wherein the detectable moieties that can be used to label PNA probes include an enzyme, such as alkaline phosphatase. Therefore, D5 is novelty destroying to claims 24(2nd) and 50.

Claims 3-12, 14-16, 20-22, 25, 29-38, 40-42, 45-47, 51 and 55-57 meet the criteria set out in Article 33(2) of the Patent Cooperation Treaty (PCT), because the closest prior art (D1, D2, D3 or D4) does not teach the technical features defined in claims 3-12, 14-16, 20-22, 25, 29-38, 40-42, 45-47, 51 and 55-57.

B. Inventive Steps

Claims 1, 2, 13, 17-19, 23, 24 (1st), 26-28, 39, 43, 44, 48, 49 and 52-54 lack an inventive step and do not comply with Article 33(3) of the *Patent Cooperation Treaty (PCT).* D6 describes a method in that the conformational changes in synthetic peptides including negatively charged peptides, positively charged peptides and neutrally charged peptides can be detected by the optical measurement of the emission spectra of a photoactive polythiophene derivative added to the peptides. D6 does not describe the use of peptide nucleic acids as capture probes. However, D9 and D10 separately describe the use of peptide nucleic acids as capture probes for the detection of nucleic acids. Thus claims 1, 2, 13, 17-19, 23, 24 (1st), 26-28, 39, 43, 44, 48, 49 and 52-54 lack inventive steps in light of the teaching of D6 in combination with D9 or D10 (Art 33(3) PCT).

Claims 1, 2, 13, 17-19, 23, 24 (1st), 26-28, 39, 43, 44, 48, 49 and 52-54 lack an inventive step and do not comply with Article 33(3) of the *Patent Cooperation Treaty (PCT).* D7 and D8 separately describe a method for the fluorometric (D7) or optical and electrochemical (D8) detection of nucleic acids using DNA probes. The method is based on the different electrostatic interactions between the water-soluble, cationic polythiophene derivatives and the single-stranded or double-stranded (hybridized) oligonucleotides. D7 and D8 do not describe the use of peptide nucleic acids as capture probes. However, D9 and D10 separately describe the use of peptide nucleic acids as capture probes for the detection of nucleic acids. Therefore, it would be obvious for a person skilled in the art to substitute the DNA probes of D7 or D8 with the peptide nucleic acid probes of D9 or D10. Having done so, said person would have a reasonable expectation of success of arriving at the subject matter of Claims 1, 2, 13, 17-19, 23, 24 (1st), 26-28, 39, 43, 44, 48, 49 and 52-54.

Claims 3-12, 14-16, 20-22, 25, 29-38, 40-42, 45-47, 51 and 55-57 lack an inventive step and do not comply with Article 33(3) of the *Patent Cooperation Treaty (PCT).* Claims 1, 2, 13, 17-19, 23, 24 (1st and 2nd), 26-28, 39, 43, 44, 48-50 and 52-54, on which claims 3-12, 14-16, 20-22, 25, 29-38, 40-42, 45-47, 51 and 55-57 depend respectively, are anticipated in view of the disclosure of D1, D2, D3, D4 or D5 respectively. Since these dependent

(Continuation on Supplemental Box)

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Box V (page 3 of 3)

claims 3-12, 14-16, 20-22, 25, 29-38, 40-42, 45-47, 51 and 55-57 only refer to standard techniques that are routinely used in a laboratory these claims lack an inventive step having regard to D1, D2, D3, D4 or D5 in combination with common general knowledge.

D11 describes the specific detection of a few hundred molecules of genetic material using a fluorescent polythiophene biosensor. Therefore, D11 would become relevant with respect to the inventive steps of claims 1-57 under Article 33(3) of the *Patent Cooperation Treaty (PCT)* if the priority claim is found to be invalid.

C. Industrial Applicability

Claims 1-57 have industrial applicability as defined under Article 33(4) of the *Patent Cooperation Treaty (PCT)*.